Backbone-Rigidified Oligo(*m*-phenylene ethynylenes)

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Abstract: Oligo(*m*-phenylene ethynylenes) (oligo(*m*-PE)) with backbones rigidified by intramolecular hydrogen bonds were found to fold into well-defined conformations. The localized intramolecular hydrogen bond involves a donor and an acceptor from two adjacent benzene rings, respectively, which enforces globally folded conformations on these oligomers. Oligomers with two to seven residues have been synthesized and characterized. The persistence of the intramolecular hydrogen bonds and the corresponding curved conformations were established by ab initio and molecular mechanics calculations, 1D and 2D ^{1}H NMR spectroscopy, and UV spectroscopy. Pentamer **5**, hexamer **6**, and heptamer **7** adopt well-defined helical conformations. Such a backbone-based conformational programming should lead to molecules whose conformations are resilient toward structural variation of the side groups. These *m*-PE oligomers have provided a new approach for achieving folded unnatural oligomers under conditions that are otherwise unfavorable for previously described, solvent-driven folding of *m*-PE foldamers. Stably folded structures based on the design principle described here can be developed and may find important applications.

Introduction

Unnatural oligomers that fold into well-defined secondary structures (foldamers) have attracted intense interest in recent years.[1−9] Most of the recently described foldamers involve helical conformations that are inspired by the helical and multiple helical structures found in nature.[10] Examples of helical foldamers include β-peptides reported by Gellman[11] and Seebach,[12] γ-peptides by Hanessian[13] and Seebach,[14] δ-peptides by Gervay[15] and Fleet,[16] peptoid oligomers described by Zuckermann and Barron,[17] pyridine−pyrimidine oligomers and helical polyheterocyclic strands by Lehn,[18] oligo(pyridine dicarboxamides) by Lehn and Huc,[19] oligoanthrilamides by Hamilton,[20] helicates by Lehn,[21] aromatic δ-peptides by Huc,[22] oxa-peptides by Yang and Wu,[23] and N,N′-linked oligoureas by Guichard.[24] Many other folding oligomers involving unnatural backbones, such as aedamers developed by Iverson,[25] N,N-linked oligoureas by Nowick,[26] vinylogous peptides by Schreiber,[27] sulfonopeptides by Gennari,[28] oligocarbamates by

Schultz,[29] oligopyrrolidones by Smith,[30] anthracene-adduct based oligomers by Winkler,[31] and alkoxy-substituted *ortho*-phenylene ethynylene oligomers by Tew,[32] have also been reported.

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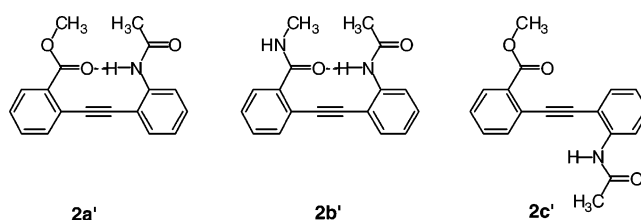(10) Rowan, A. E.; Nolte, R. J. M. *Angew. Chem., Int. Ed.* **1998**, *37*, 63.

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Moore et al. established an elegant helical foldamer system based on solvent-driven folding of helical oligo(*m*-phenylene ethynylenes) (oligo(*m*-PE)).[33] By attaching polar side chains to oligo(*m*-PE) backbones, the resultant oligomers were found to adopt well-defined conformations in polar solvents. For these *m*-PE oligomers, folding was effected by the solvaphobic nature of the PE backbone and the solvaphilicity of the polar side chains. In nonpolar solvents such as chloroform, these PE oligomers were found to be random coils. The *meta*-substituted

benzene rings introduce a curvature into the *m*-PE backbones, which results in helical conformations for oligomers consisting of greater than six phenylene ethynylene residues. Different from many other foldamer systems, these helical PE oligomers contain a hydrophobic cavity of ∼8 Å across. Studies showed that the hydrophobic cavities can serve as hosts for a variety of organic molecules in polar solvents.

We have developed helical foldamers based on a strategy of backbone-rigidification.[5,34] By incorporating intramolecular H-bonds along the backbone of aromatic oligoamides, we obtained oligomers whose backbones were forced to adopt crescent or helical conformations. By tuning the curvature of the backbone-rigidified oligoamides, nanosized cavities of 10 and 30 Å across have been created. Large cavities or channels, which are usually found at the tertiary and quaternary structural level of biopolymers, have been realized in few unnatural foldamer systems. Our folding oligoamides, along with the helical foldamers described by Lehn[18] and Moore,[33] represent one of the few helical foldamer systems with large cavities. Besides, our crescent oligoamide system also allows the tuning of cavity sizes.

It is known that a very small barrier (∼0.6 kcal/mol) exists for the internal rotation of diphenylacetylene.[35] As a result, the conformations of simple *o*- and *m*-PE oligomers and polymers are expected to be very flexible and random. By incorporating an intramolecular H-bond into diphenylacetylene, the resulting **2a′** should adopt a well-defined conformation that is enforced by this additional noncovalent interaction. Indeed, Kemp reported that diphenylacetylene such as **2b′**, with its intramolecular H-bond, adopted a H-bonded conformation and could serve as *β*-turn mimetics.[36] Introducing such intramolecular H-bonding interactions into longer *m*-PE oligomers should thus limit the internal rotation of the backbone, leading to well-defined (folded) conformations.

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2a'   **2b'**   **2c'**

We reported our preliminary studies on folding *m*-PE oligomers based on backbone-rigidification.[34b] By introducing intramolecular H-bonds along the *m*-PE backbones, *m*-PE oligomers adopting well-defined, folded conformations in the nonpolar chloroform were obtained. Depending on chain length, crescent and helical conformations with a well-defined cavity

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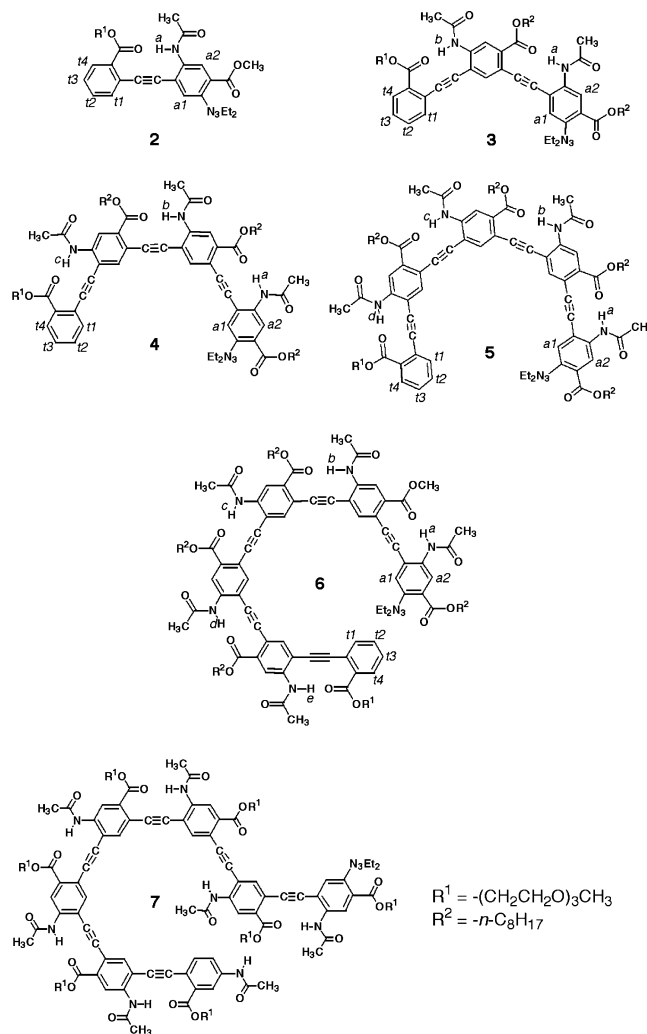(36) Kemp, D. S.; Li, Z. Q. *Tetrahedron Lett.* **1995**, *36*, 4175.

of 8 Å in diameter were obtained. Moore et al. also described that introducing one intramolecular H-bond into long *m*-PE oligomers led to enhanced stability.[33a] As compared to the solvent-driven PE foldamers established by the Moore group, the folding of our backbone-rigidified *m*-PE oligomers is based on a different mechanism that involves intramolecular H-bonds incorporated into the backbone. The effects of solvents on the folding of our PE oligomers are thus opposite to those of the Moore system: In nonpolar solvents such as chloroform, our PE oligomers are stably folded due to the presence of intramolecular H-bonds, while the PE foldamers described by Moore are folded in polar solvents and denatured in chloroform.

In this Article, we describe the detailed design, preparation, and characterization of a series of our backbone-rigidified *m*-PE oligomers. Specifically, oligomers **2**, **3**, **4**, **5**, **6**, and **7** containing two, three, four, five, six, and seven benzene rings, respectively, were designed on the basis of these considerations: (1) To facilitate the comparison of chain-length-dependent changes by 1D and 2D NMR, the two different termini of each of the oligomers were designed to be consistent across this series of oligomers, which allows the "terminal" aromatic protons *t1*–*t4* and *a1*–*a2* to be directly comparable among the oligomers. (2) The carbonyl oxygen atoms of benzoate ester groups should act as the acceptors for intramolecular H-bonds. Ester groups were chosen to avoid any potential steric hindrance that may exist between the benzamide proton (or large N-substituent) and the neighboring aromatic protons. (3) Finally, benzoate ester groups were chosen on the basis of the long-term consideration of preparing a variety of oligomers with different side chains via simple transesterification reactions.

Oligomers **2**–**6** were examined by computational studies, ^{1}H NMR, and UV spectroscopy. The results obtained are fully consistent with the expected H-bonded conformations. The newly synthesized heptamer **7** has been characterized by ^{1}H NMR, mass spectometry, and UV spectroscopy. The successful development of this new foldamer system based on the PE backbone, along with the system we developed before, demonstrates that backbone-rigidification by noncovalent interactions should be applicable to a variety of different oligomers, leading to foldamers with different properties and applications.

Results and Discussion

Synthesis. The synthesis of monomer building blocks is shown in Scheme 1. Methyl 3-nitrobenzoate was hydrogenated in the presence of acetic anhydride to give **1a**, which was nitrated to give **1b**. Compound **1b** was then deprotected with H_2SO_4 in methanol, and the product **1c** was converted into **1d** by iodination. Treating **1d** with acetic anhydride in the presence of H_2SO_4 in CH_2Cl_2 led to **1e** that was reduced to **1f**. Conversion of **1f** into **1g** was realized by treating **1f** with HNO_2 followed by Et_2NH. Pd-catalyzed Sonogashira coupling[37] of **1g** with (trimethylsilyl)acetylene gave **1j** which was converted to iodide **1l** using methyl iodide.[38] Compound **1g** was then converted to the octyl ester **1i** by hydrolysis followed by esterification with

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octanol. Coupling **1i** with (trimethylsilyl)acetylene gave **1k**, which was converted into **1m** and **1n** by hydrolysis and treatment with methyl iodide. Based on monomers **1l**, **1m**, and **1n**, oligomers **2**–**6** were synthesized by Sonogashira coupling reactions.
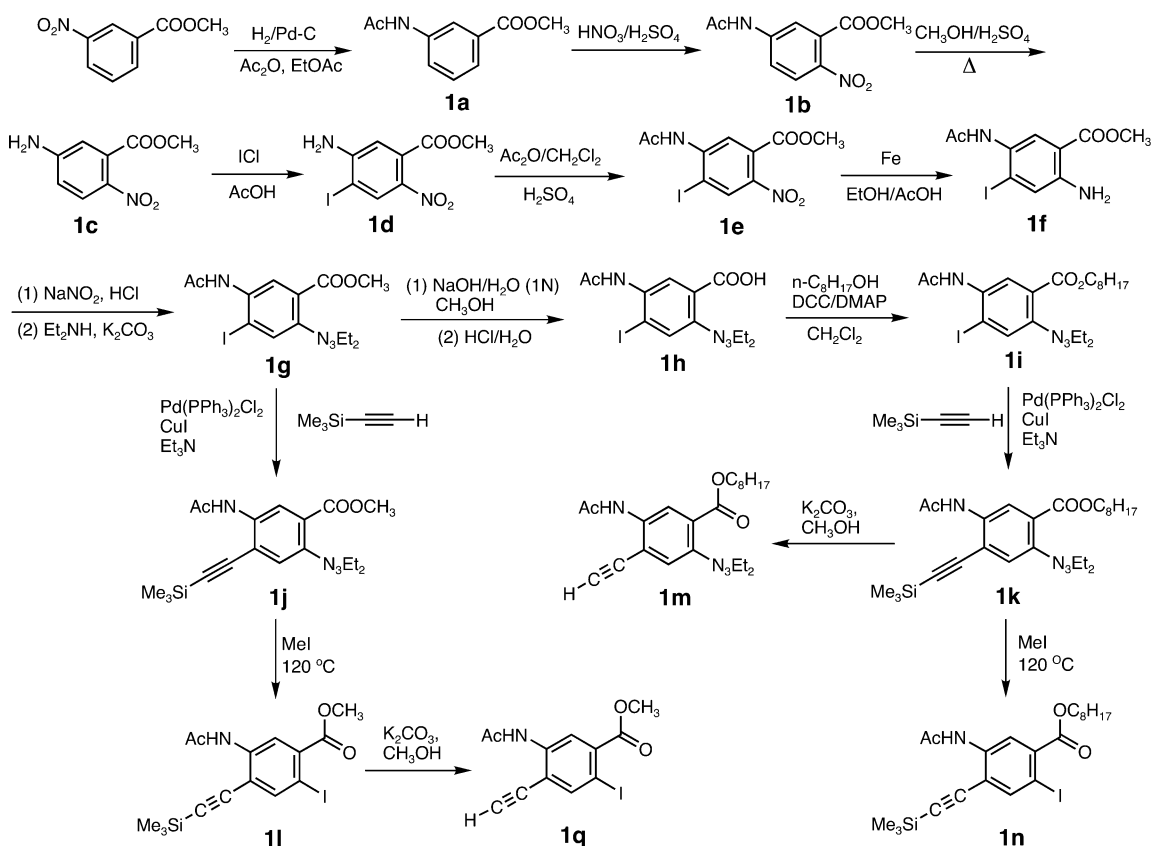
As shown in Scheme 2, coupling **1m** and **1n** led to dimer **2e** that was deprotected to give **2f**. Treating **2f** with ester **1p**, which was obtained from the commercially available acid **1o**, resulted in trimer **3**. Dimer **2** was obtained by coupling **1p** with **1l**. Treating **3** with methyl iodide led to the iodide **3a**. Trimer **3a** was then converted to tetramer **4** and pentamer **5** by coupling with **1m** and **2f**, respectively.

Scheme 3 shows the preparation of hexamer **6**. To increase the ^{1}H NMR signal dispersion of **6** and to test a strategy of segment condensation involving longer intermediates, hexamer **6** was synthesized by first preparing another trimeric intermediate **3c**. Coupling **1l** and **1m** gave dimer **2g**, which was hydrolyzed to **2h**. Trimer **3c** was obtained by hydrolyzing **3b**, which in turn was from coupling **2h** with **1n**. The Pd-catalyzed coupling of trimers **3c** and **3a** went smoothly, leading to hexamer **6** in 73% yield.
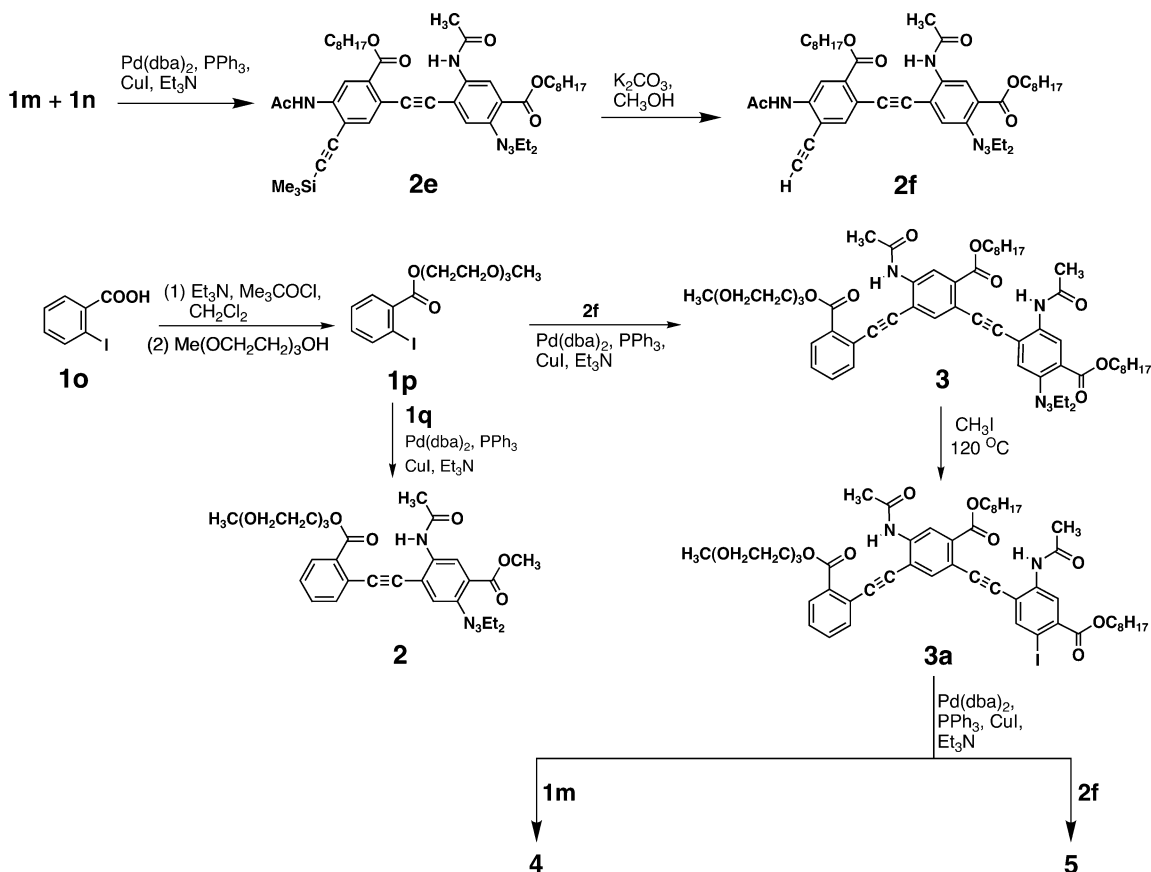
Heptamer **7** was prepared in 22% yield by coupling dimer **2i** and pentamer **5a**, which in turn were prepared on the basis of similar procedures used for preparing **2f** and **5** (Scheme 4). The reaction conditions for preparing **7** are being optimized to achieve a better yield.
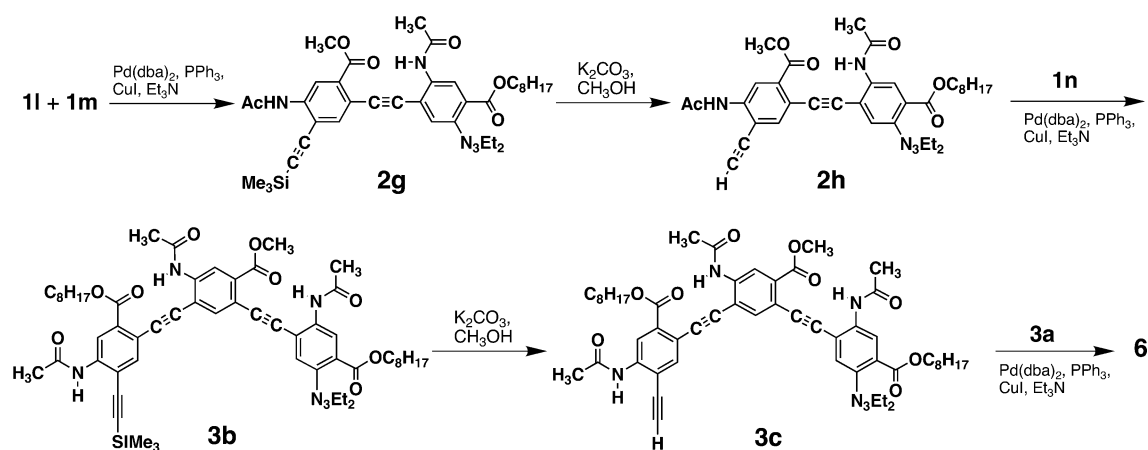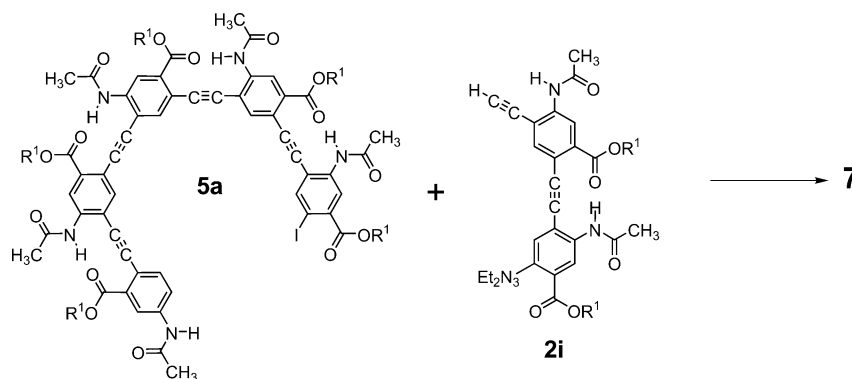
Scheme 1

Scheme 2

Computational Studies. We previously demonstrated results from ab initio molecular orbital calculations[39] that **2a′** adopted a completely planar conformation due to the presence of the intramolecular H-bond in its structure.[34b] This result was

Scheme 3

1l + 1m → (Pd(dba)$_2$, PPh$_3$, CuI, Et$_3$N) **2g** → (K$_2$CO$_3$, CH$_3$OH) **2h** → **1n** (Pd(dba)$_2$, PPh$_3$, CuI, Et$_3$N) →

3b → (K$_2$CO$_3$, CH$_3$OH) **3c** → **3a** (Pd(dba)$_2$, PPh$_3$, CuI, Et$_3$N) → **6**

Scheme 4

5a + **2i** → **7**

supported by the X-ray structure of a dimer. A more detailed calculation indicated that interrupting the intramolecular H-bond of **2a′** by rotating around one of the C–Ph bonds led to the conformation **2c′** which was significantly less stable. Deviation from the planar conformation by distorting and eventually interrupting the intramolecular H-bond led to a rapid increase in energy. An energy difference of 5.78 kcal/mol was found between optimized conformer **2a′** and optimized conformer **2c′**. A rotational barrier of 7.19 kcal/mol exists between optimized **2a′** and unoptimized **2c′** (Figure 1), suggesting that the H-bonded **2a′** should be overwhelmingly favored over other conformations that involve the interruption of the intramolecular H-bonds.

To probe the conformations of longer oligomers, molecular mechanics calculations (MM3 force field) were carried out on analogues of **4**, **5**, **6**, and **7**. Figure 2 shows the energy-minimized conformations of these four oligomers. The tetramer adopts a planar, crescent conformation that is rigidified by intramolecular H-bonds (Figure 2a). The pentamer, on the other hand, adopts a helical conformation already (Figure 2b). Although the PE backbone of the pentamer is not long enough for it to adopt a helical conformation, the presence of the
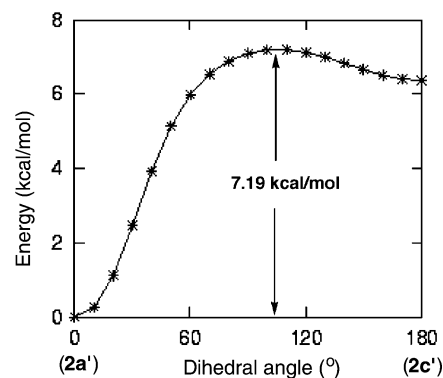
(39) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Rega, N.; Salvador, P.; Dannenberg, J. J.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.11; Gaussian, Inc.: Pittsburgh, PA, 2002.

Figure 1. The energy of the various conformers between **2a′** and **2c′** as a function of the degree of rotation about the Ph–C bond.

diethyltriazenyl group adds additional length, leading to a helical conformation in which the two methyls of the diethyltriazenyl group and the other end of the molecule are brought into close proximity. The hexamer, in combination with its diethyltriazenyl tail, is long enough to adopt a helical conformation (Figure 2c). In this conformation, the diethyltriazenyl group overlaps more significantly with the other end of the molecule. The backbone of the heptamer is long enough, which allows a stacking interaction between the terminal aromatic rings (Figure 2d). A helical pitch of ~3.4 Å is observed for this heptamer.

One-Dimensional (1D) ^{1}H NMR Spectroscopy. In chloroform, the ^{1}H NMR spectrum of heptamer **7** shows extensive signal-overlap and line-broadening, which prevents proper assignment of the spectrum. Therefore, only the ^{1}H NMR spectra of oligomers **2–6** are compared. In Table 1, the chemical shift values of the amide ^{1}H signals of **1k** and oligomers **2–6** are
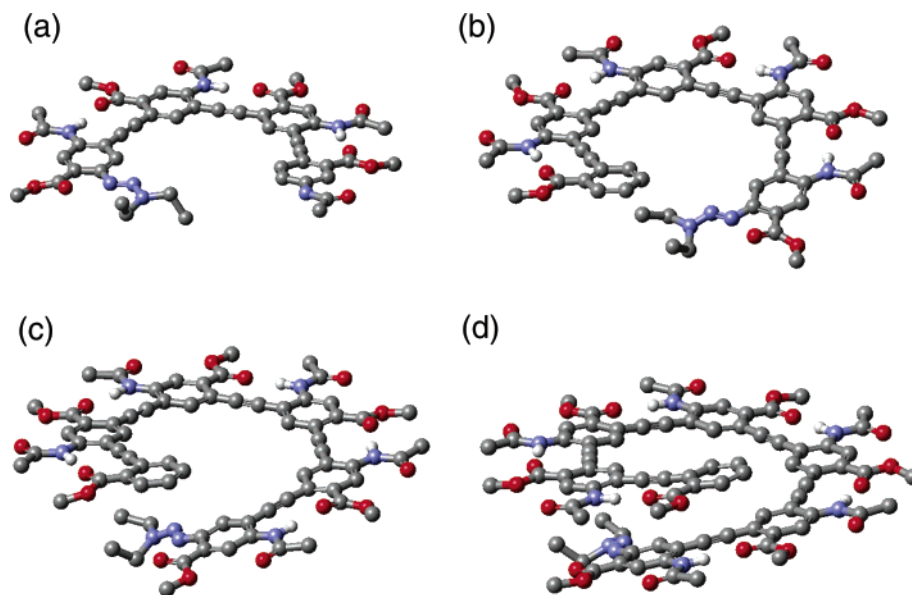
Figure 2. The energy-minimized (MM3 force field) conformations of (a) a tetramer, (b) a pentamer, (c) a hexamer, and (d) a heptamer with their backbones corresponding to **4**, **5**, **6**, and **7** with methyls on the ester side chains.
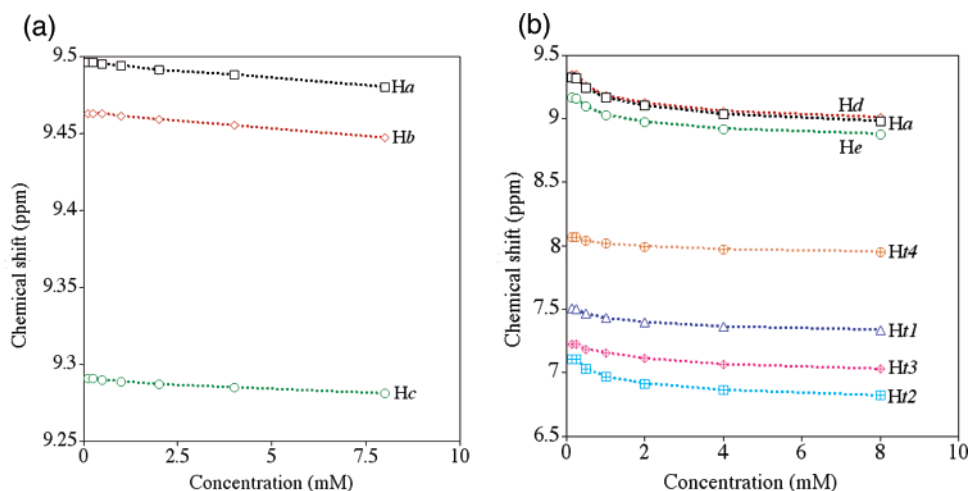

Figure 3. Concentration-dependent changes of ^{1}H chemical shifts of (a) amide protons **4** and (b) amide protons *a*, *d*, and *e*, and aromatic protons *t1*−*t4* of **6**.

Table 1. Chemical Shifts of Amide Protons^a

oligomer	H*a*	H*b*	H*c*	H*d*	H*e*
6	9.11	9.45	9.44	9.11	8.98
5	9.48	9.46	9.43	9.28	
4	9.49	9.46	9.29		
3	9.45	9.27			
2	9.27				
1k	7.92				

^{a} Measured at room temperature, 1 mM in CDCl$_3$ (500 MHz).

listed. As compared to the chemical shift of the amide proton of **1k**, which cannot form any intramolecular H-bond, the amide protons of oligomers **2**−**6** showed significant (>1 ppm) downfield shifts, consistent with the expectation that these NH groups are involved in intramolecular H-bonding interactions.

Upon diluting a sample of tetramer **4** from 8 to 0.125 mM (CDCl$_3$, 295 K, 500 MHz), the three NH signals of **4** show very small downfield shifts of 0.016 (H*a*), 0.016 (H*b*), and 0.01 (H*c*) ppm, respectively (Figure 3a), typical of amide protons involved in intramolecular H-bonding interactions. Similar to

those of **4**, the amide protons H*a*, H*d*, and H*e* of hexamer **6** also demonstrate downfield shifts from 8 to 0.125 mM (Figure 3b). However, unlike the small shifts of the NH signals of tetramer **4**, the three resolved NH signals of **6** show much larger concentration-dependent shifts of 0.344 (H*a*), 0.338 (H*d*), and 0.287 (H*e*) ppm. The downfield shifts of the NH groups upon diluting the solution of **4** or **6** suggest that they are not involved in intermolecular H-bonding, because interrupting intermolecular H-bonds should lead to upfield, rather than downfield, shifts of the NH signals. Instead, these downfield shifts of NH signals are consistent with the interruption of intermolecular π−π stacking interactions at low concentrations. That the observed changes in the shifts of amide protons are not related to H-bonding is further confirmed by examining aromatic protons *t1*−*t4* of **6**. From 8 to 0.125 mM, protons *t1*−*t4* showed the same nonlinear, downfield shifts as those of amide protons *a*, *d*, and *e*, indicating that the observed shifts of the amide protons were not due to H-bonding.

Variable-temperature ^{1}H NMR measurements (2 mM, CDCl$_3$, 500 MHz) of the amide proton signals of tetramer **4** and hexamer **6**
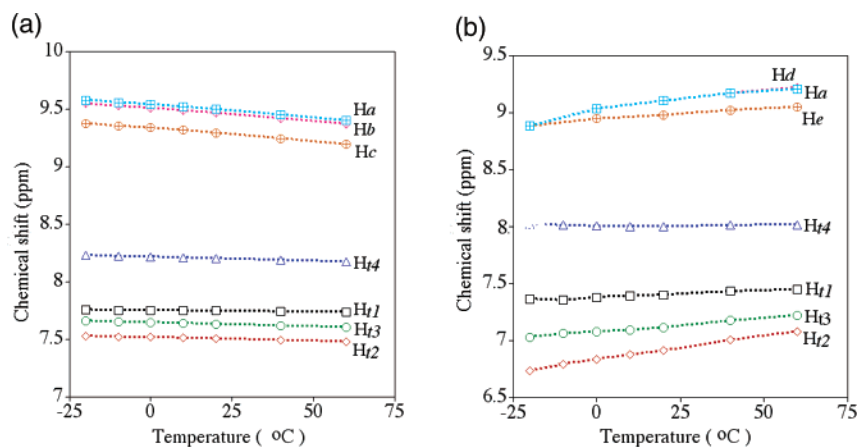
Figure 4. Temperature-dependent changes of ^{1}H chemical shifts of the amide and terminal aromatic protons of (a) tetramer **4** and (b) hexamer **6**.
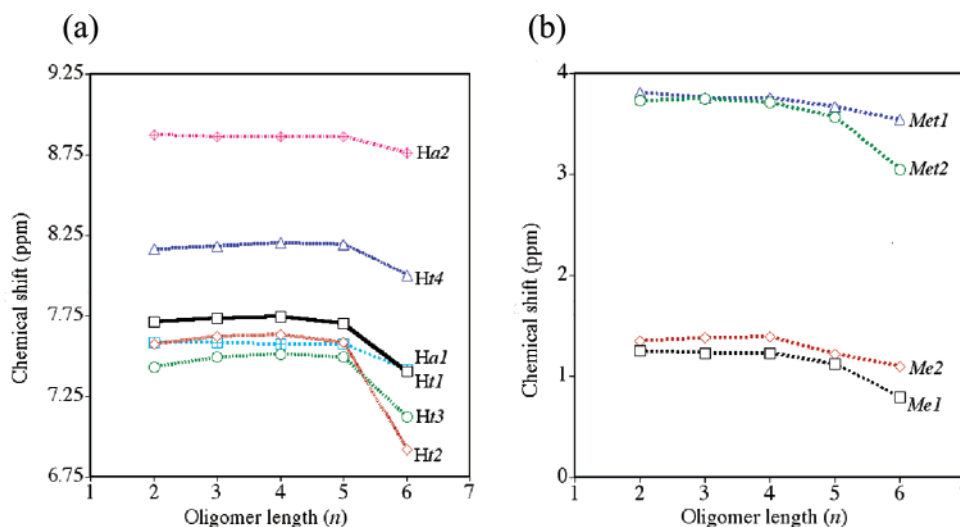

Figure 5. ^{1}H chemical shifts (1 mM, CDCl$_3$, 500 MHz, 295 K) of (a) protons *t1*−*t4* and *a1*−*a2* versus chain length of oligomers **2**−**6**, and (b) the methyl (*Me1* and *Me2*) and methylene (*Met1* and *Met2*) protons of the diethyltriazenyl group.

6 provided additional evidence for the prevalence of intramolecular H-bonds (Figure 4). From −20 to 60 °C, the three amide NH signals of **4** show small upfield shifts of −2.25 × 10^{-3} (H*a*), −2.23 × 10^{-3} (H*b*), and −2.29 × 10^{-3} (H*c*) ppm/K (Figure 4a). These values are typical of intramolecular H-bonding.[34d,40] In comparison, aromatic protons *t1*−*t4* have almost no temperature-dependent change. Instead of moving upfield, the amide NH protons *a*, *d*, and *e* of hexamer **6** showed downfield shifts of 4.06 × 10^{-3} (H*a*), 4.25 × 10^{-3} (H*d*), and 2.07 × 10^{-3} (H*e*) ppm/K, as the temperature was raised (from −20 to 60 °C in CDCl$_3$) (Figure 4b). A similar trend of temperature-dependent downfield shifts is associated with the aromatic protons *t1*−*t3* of **6**, suggesting that the observed shifts of amide protons are not due to the interruption of intramolecular H-bonding. These observations are most likely the results of two opposite trends: (1) the small upfield shifts of the intramolecularly H-bonded amide protons of **6** as the temperature was raised, and (2) the downfield shifts of almost all of the protons of **6** due to the disruption of intermolecular aromatic stacking interactions at elevated temperatures. Obviously, between the two trends, interruption of the intermolecular interaction at elevated temperatures played the dominant role in affecting the ^{1}H chemical shifts of hexamer **6**.

(40) Gong, B.; Yan, Y.; Zeng, H.; Skrzypczak-Jankunn, E.; Kim, Y. W.; Zhu, J.; Ickes, H. A. *J. Am. Chem. Soc.* **1999**, *121*, 5607.

A more detailed examination revealed (Figure 4b) that the NMR signals of protons *t2* and *t3* showed obvious downfield shifts with rising temperature, proton *t1* was less sensitive, and proton *t4* showed the least change in its position. In contrast, the corresponding protons *t1*−*t4* of tetramer **4** all showed almost no temperature-dependent shifts. This suggests that the end protons *t1*−*t4* of **6** are located in a local environment that is different from those of other shorter oligomers such as **4**. Most likely, this local environment that is unique to **6** is due to its length and folded conformation: the backbone of **6** is long enough to bring its two ends into close proximity. Consistent with this picture, protons *t2* and *t3*, which are at the very tip of the molecule, shifted more significantly than protons *t1* and *t4*. If the observed downfield shifts of the aromatic end proton signals of **6** were due to a folded conformation, the chemical shifts of these proton signals should be sensitive to a change in temperature. The folded conformation will be partially interrupted (or "denatured") at raised temperatures, which should change (increase) the distance between the two ends and should thus cause the ^{1}H NMR signals of the end protons to move downfield. This is, as shown in Figure 4, indeed the case.

Comparing the chemical shifts of aromatic protons *t1*−*t4* and *a1*−*a2* on the termini of oligomers **2**−**6** reveals the effect of chain length on the resonances of these protons (Figure 5a). An interesting trend is observed: from dimer **2** to tetramer **4**,
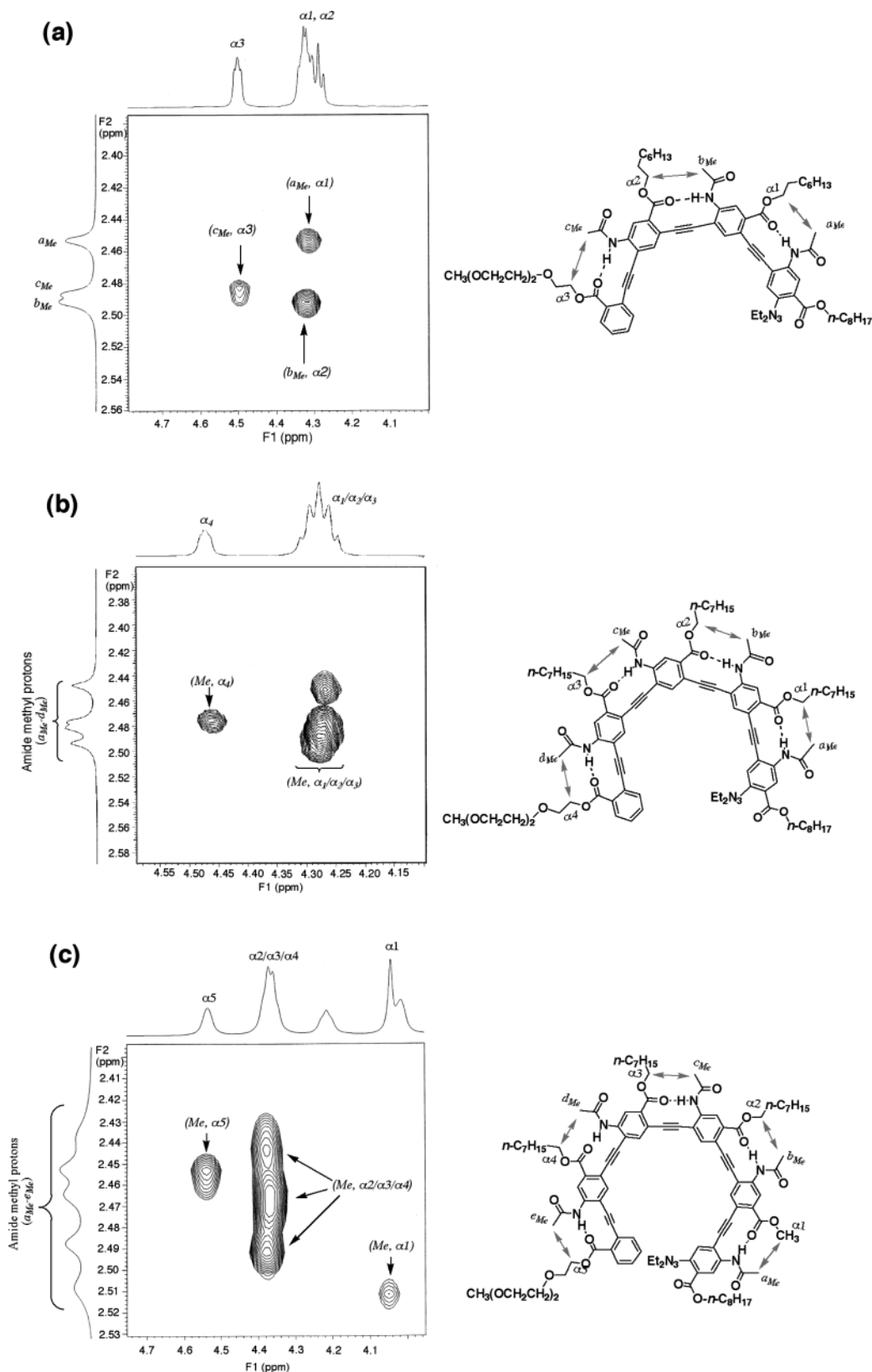
Figure 6. Partial NOESY spectra **4** (8 mM in CDCl$_3$, 500 MHz, 263 K, mixing time: 0.3 s) revealing the side-chain NOE contacts of (a) tetramer **4**, (b) pentamer **5**, and (c) hexamer **6**. The contacts between ester protons (α) and the amide methyl protons are shown in the structures. These contacts are indicated by arrows in the spectrum.

the chemical shifts of protons *a1*−*a2* and *t1*−*t4* show very little changes. In contrast, the end protons of pentamer **5** move slightly upfield as compared to those of **2**−**4**. As compared to **5**, the corresponding protons of hexamer **6** have shifted significantly

to upfield positions. The shifts are particularly substantial (up to 0.5 ppm) for protons *t2* and *t3*. The same trend of upfield shifts is observed for the methyl (*Me1* and *Me2*) and methylene (*Met1* and *Met2*) protons of the diethyltriazenyl groups (Figure
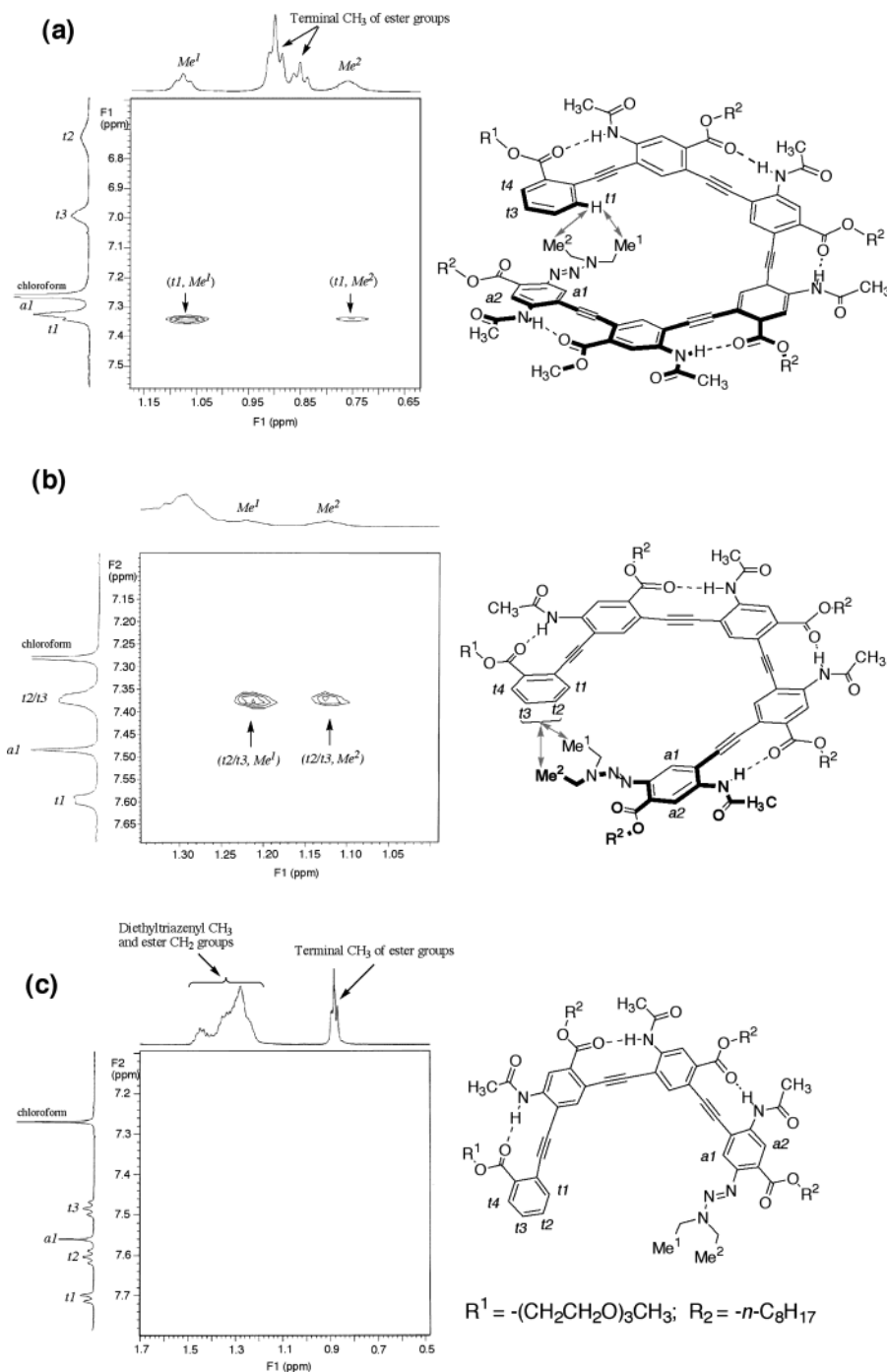
Figure 7. Partial NOESY spectra **4** (8 mM in CDCl₃, 500 MHz, 263 K, mixing time: 0.3 s) revealing the presence of end-to-end NOE contacts in (a) hexamer **6** (8 mM in CDCl₃, 500 MHz, 263 K, mixing time: 0.3 s), (b) pentamer **5**, and (c) the absence of such NOEs in the spectrum of tetramer **4**. These NOEs are indicated by arrows in the spectrum.

5b): while those of **2−4** remain constant, those of **5** and **6** show upfield shifts. Shifts up to 0.7 ppm are observed for the methyl protons. These results can only be explained by the corresponding oligomer's adopting a curved backbone: while oligomers **2−4** are not long enough, pentamer **5** is long enough for its two termini to approach (or "feel") each other; hexamer **6** reaches a length which, in combination with its rigidified (curved) backbone, allows its two otherwise remote termini to be brought into close proximity. This folded conformation caused the pronounced upfield shifts[41] of the corresponding aromatic protons on the two termini of **6**.

Two-Dimensional (2D) NMR Spectroscopy. Tetramer **4** was first examined by 2D (NOESY) ¹H NMR studies (Figure 6a). The three acetamido methyl signals, a_{Me}, b_{Me}, c_{Me}, appear at 2.449, 2.483, and 2.487 ppm as three peaks, two of which partially overlapped each other. The NOEs (indicated by arrows) are well separated in the NOESY spectrum. These NOEs include the side-chain contacts between protons a_{Me}, b_{Me}, and c_{Me} of the acetamido methyl groups and the α-CH₂ groups ($\alpha 1$, $\alpha 2$, and $\alpha 3$) of the ester side chains.

(41) Perkins, S. J. *Biol. Magn. Reson.* **1982**, *4*, 193.
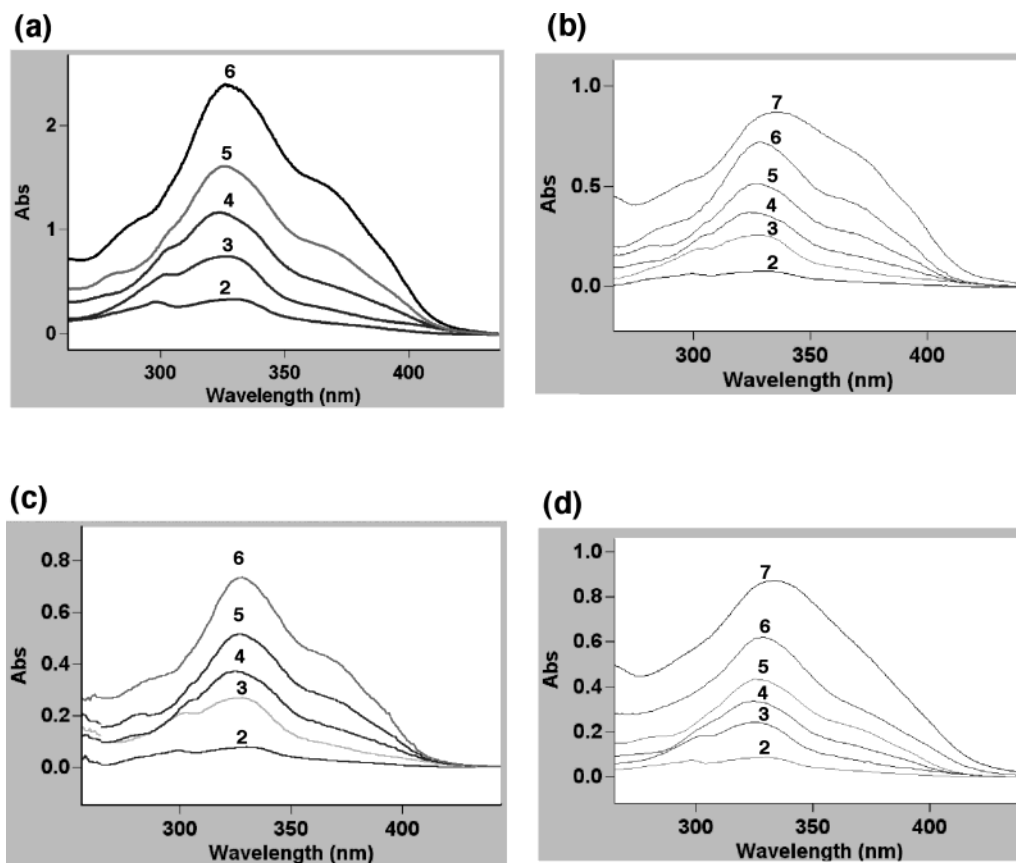
Figure 8. UV spectra of (a) **2**−**6** at 10 μM in chloroform; (b) **2**−**7** at 2 μM in chloroform; (c) **2**−**6** at 2 μM in chloroform at 60 °C; (d) **2**−**7** at 2 μM in chloroform/methanol (v/v 1/1).

For pentamer **5**, NOEs between the acetamido methyl protons (a_{Me}, b_{Me}, c_{Me}, and d_{Me}) and the α-methylene protons of the ester groups are observed (Figure 6b). Unfortunately, the ^{1}H signals of the α-methylene groups $\alpha2$, $\alpha3$, and $\alpha4$ overlap. As a result, only two, instead of the expected three, NOE cross-peaks are detected. Another cross-peak that is well separated represents the contact between the protons of methyl d_{Me} and methylene $\alpha4$. Although signal overlap prevents the NOEs from being clearly assigned to individual side-chain contacts, the number and intensities of the detected NOEs are consistent with the expected four amide−ester side-chain contacts. Among the three NOEs, the intensity of the largest cross-peak is about twice those of the other two, indicating that this largest cross-peak is the result of two sets of amide−ester contacts.

Among the five ester α-methylene groups of **6**, the ^{1}H signals of three ($\alpha2$−$\alpha4$) overlap in the corresponding 1D NMR spectrum. Nevertheless, the five amide−ester side-chain NOE contacts of hexamer **6** are clearly discerned by NOESY. These correspond to the side-chain−side-chain contacts between the protons of the five acetamido methyl groups (a_{Me}, b_{Me}, c_{Me}, d_{Me}, and e_{Me}) and the five ester α-methylene groups ($\alpha1$−$\alpha5$) of the ester groups (Figure 6c). No attempts were made to assign all of the NOEs to their corresponding contacts.

These side-chain NOE contacts are consistent with the existence of the intramolecular H-bonds, which are consistent with curved conformations adopted by oligomers **4**, **5**, and **6**.

In the NOESY spectrum of **4**, NOEs between the three amide protons a, b, and c and the ester α-CH$_2$ groups are also observed (data not shown). In the NOESY spectra of **5** and **6**, NOEs

between the amide NH protons and the protons of the ester side chains could not be clearly identified due to overlap of the signals.

Comparing the NOESY spectrum of **4** to that of **5** or **6** revealed a significant difference (Figure 7): NOEs between protons of the two diethyltriazenyl methyl groups (Me^1 and Me^2) and proton $t1$ of **6** (Figure 7a), or between protons of Me^1 and Me^2 and $t2$ (or $t3$ or both) of **5** (Figure 7b), are observed. These NOEs are absent in the NOESY spectrum of **4** (Figure 7c). Although the upfield shifts of protons $a1$ and $t1$ of **6** lead to the overlap of their ^{1}H NMR signals, the observed NOEs can only be those between proton $t1$ and the protons of Me^1 and Me^2. The reason is that in the NOESY spectrum of either **4** or **5**, no NOEs are observed between proton $a1$ and those of Me^1 and Me^2. The end-to-end NOEs observed for **5** and **6** provide additional convincing evidence for the proposed, rigidified backbones of these oligomers. The backbone of **4** is too short for its two ends to be in close proximity. As results from the above molecular mechanics calculation show, pentamer **5** already adopts a helical conformation due to the presence of the diethyltriazenyl group. This is confirmed by the detection of NOEs between the methyl protons and proton $t2$ or $t3$. Consistent with its longer backbone, hexamer **6** brings its two ends into close proximity in such a way that the end-to-end contacts are now between proton $t1$, instead of proton $t2$ or $t3$ (as for pentamer **5**), and those of Me^1 and Me^2. To place Me^1 and Me^2 closer to $t1$ rather than to $t2$ and $t3$, hexamer **6** must adopt a helical conformation, which is fully consistent with the above results from computational and 1D NMR studies.

UV Spectroscopy. The UV spectra of oligomers **2**–**7** in chloroform are shown in Figure 8. Each of the six compounds shows a very strong absorption band at ~330 nm. The shapes of the spectra of dimer **2**, trimer **3**, and tetramer **4** are very similar. However, a new band appears for pentamer **5** at ~370 nm and more so for hexamer **6**. The 370-nm shoulder for **5** or **6** should not be due to intermolecular interaction because the concentrations used for measuring the UV spectra are already very low (Figure 8a, 10 μM) and diluting the samples to 2 μM led to a set of spectra of nearly identical shapes (Figure 8b). Recording the UV spectra at an elevated temperature (60 °C) only slightly weakened the 370-nm bands of **5** and **6** (Figure 8c). In spectra recorded in the mixed solvent of chloroform/methanol (1:1), the shapes of the spectra of **2**–**4** remain unchanged in this mixed solvent (Figure 8d). The presence of methanol in chloroform should weaken the intramolecular H-bonds and may thus disturb the folded conformations. Indeed, the 370-nm bands of **5** and **6** are greatly diminished. Considering the structural similarity between oligomers **2**–**6**, these UV results suggest that the 370-nm shoulders of **5** and **6** in chloroform seem to be associated with their two termini that are brought into close proximity by the corresponding folded conformation.

The 370-nm bands are thus very likely the results of exciton coupling between the two termini, which act as two component chromophores, each of **5** and **6**. Thus, the closer the two termini are in an oligomer, the more obvious (or stronger) this band may become. If this is the case, the 370-nm band should be enhanced in the UV spectra of PE oligomers longer than **5** and **6**. This expectation is confirmed by the UV spectrum of the newly synthesized heptamer **7**. In chloroform, the 370-nm band is further enhanced in the spectrum of **7** and, similar to **5** and **6**, is significantly weakened in the presence of 50% methanol in chloroform. This band at 370 nm could serve as a convenient spectroscopic means for the rapid assay of the folding of higher homologues . For oligomers carrying chiral side-chain groups that induced the twist sense bias in the backbones, exciton coupling can be detected even more clearly using CD spectroscopy.

Conclusions

Strong intramolecular H-bonds act to rigidify the otherwise flexible conformations of oligo(*m*-phenylene ethynylenes), leading to folded conformations from the dimer up. This study has demonstrated the feasibility of designing backbone-rigidified PE oligomers with stably folded, crescent or helical conformations. Extending the design principle to longer oligomers and polymers is the obvious next step. Furthermore, by incorporating building blocks with the two ethynyl linkages being placed in a *para*-geometry on the same benzene ring, the curvature of the backbones can be adjusted. This, combined with the localized nature of backbone-rigidification, allows the development of PE helices with larger interior cavities. This new class of PE foldamers, with their unsaturated (fluorescent) backbones, is reminiscent of helicenes.[42] By incorporating chiral side chains, it should be possible to control the twist sense bias of oligomers with lengths over one helical turn. Helical materials with interesting chiroptical properties may result. A more exciting prospect involves the well-defined, large hydrophobic cavities

generated. A variety of applications, for example, the design of novel hosts, sensors, and porous materials, can be envisaged.

Experimental Section

General. All chemicals were purchased from Aldrich or Acros and were used as received unless otherwise noted. Triethylamine was dried from sodium and degassed before use. The coupling reactions were carried out under dry argon. All reactions were followed by thin-layer chromatography (precoated 0.25 mm silica gel plates from Aldrich), and silica gel column chromatography was carried out with silica gel 60 (mesh 230-400). All ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Unity INOVA-500 spectrometer (500 MHz). NMR chemical shifts are reported in ppm relative to internal standard TMS, and the coupling constant, J, is reported in hertz (Hz). The following splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; b, broad; m, multiplet. UV spectra were recorded on a Varian Cary 50 UV–vis spectrometer.

Methyl 5-Acetylaminobenzoate (1a). Compound **1a** was synthesized starting from commercially available 3-nitrobenzoic acid which was initially esterified (98.9%) followed by reduction of the nitro group and protection of the corresponding amino group using acetic anhydride (94.3%) to afford a white solid. TLC, $R_f = 0.40$ (petroleum ether/EtOAc, 1/2). ^{1}H NMR (500 MHz, CDCl$_3$): δ 2.20 (s, 3H, Ac), 3.90 (s, 3H, MeO), 7.39 (t, 1H, Ar–H), 7.65 (s, 1H, NH), 7.78 (d, 1H, Ar–H, $J = 7.5$ Hz), 7.92 (d, 1H, Ar–H, $J = 7.5$ Hz), 8.02 (s, 1H, Ar–H).

Methyl 5-Acetamido-2-nitrobenzoate (1b). Compound **1a** (35 g, 181 mmol) was added to concentrated H$_2$SO$_4$ (120 mL) cooled in an ice–water bath. To this solution, a cooled mixture of 70% HNO$_3$ (12.3 mL) and concentrated H$_2$SO$_4$ (58 mL) was added dropwise over a period of 0.5 h at 0 °C. After being stirred for 20 min, the reaction mixture was poured into cracked ice (1 kg), and the mixture was extracted with dichloromethane (150 mL × 3). The combined extracts were then washed with aqueous NaHCO$_3$ and water, respectively, dried over anhydrous Na$_2$SO$_4$, filtered, and concentrated to provide a brown residue. The resulting solid was recrystallized from dichloromethane to afford 24 g (55.7%) of **1b** as a pale yellow needle. TLC, $R_f = 0.36$ (petroleum ether/EtOAc, 1/3). ^{1}H NMR (500 MHz, CDCl$_3$): δ 2.24 (s, 3H, Ac), 3.93 (s, 3H, MeO), 7.61 (d, 1H, Ar–H), 7.86 (dd, 1H, Ar–H), 7.94 (b, 1H, NH), 7.98 (d, 1H, Ar–H, $J = 7.5$ Hz). ^{13}C NMR (125 MHz, CDCl$_3$): δ 25.11, 54.03, 119.49, 121.18, 126.35, 130.37, 142.46, 143.55, 167.28, 167.78.

Methyl 5-Amino-2-nitrobenzoate (1c). To a solution of **1b** (2.17 g, 9.12 mmol) in MeOH (50 mL) was added concentrated H$_2$SO$_4$ (0.9 mL) with stirring. The solution was refluxed for 0.5 h, and the solvent was removed in vacuo to provide a pale yellow oil. The oil was dissolved in dichloromethane (30 mL) and washed with NaHCO$_3$, water, and brine. After being washed, the organic layer was dried over Na$_2$SO$_4$ and filtered. The filtrate was then concentrated in vacuo to yield a light yellow solid, which was recrystallized from EtOAc to afford 1.65 g (92.3%) of **1c** as a colorless solid. TLC, $R_f = 0.24$ (petroleum ether/EtOAc, 3/2). ^{1}H NMR (500 MHz, CDCl$_3$): δ 3.92 (s, 3H, MeO), 4.56 (s, 2H, NH$_2$), 6.61 (m, 2H, Ar–H), 7.94 (d, 1H, Ar–H, $J = 9.5$ Hz). ^{13}C NMR (125 MHz, CDCl$_3$): δ 53.19, 112.99, 114.31, 127.23, 132.11, 151.77, 167.54.

Methyl 5-Amino-4-iodo-2-nitrobenzoate (1d). To a vigorously stirred solution of **1c** (4.42 g, 22.6 mmol) in glacial acetic acid (20 mL) was added dropwise a solution of ICl (3.67 g, 22.6 mmol) in glacial acetic acid (5 mL). After 10 min, a yellow precipitate appeared, and the solution was allowed to stir for another 12 h. Upon completion, the yellow solution was poured into water (50 mL) and filtered to yield a yellow solid, which was recrystallized from MeOH to afford 5.7 g (78.3%) of the yellow solid **1d**. TLC, $R_f = 0.42$ (petroleum ether/EtOAc, 3/2). ^{1}H NMR (500 MHz, CDCl$_3$): δ 3.91 (s, 3H, MeO), 4.88 (b, 2H, NH$_2$), 6.73 (s, 1H, Ar–H), 8.42 (s, 1H, Ar–H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 53.57, 81.67, 94.81, 111.87, 114.38, 131.46, 136.17, 151.61.

(42) Katz, T. J. *Angew. Chem., Int. Ed.* **2000**, *39*, 1921.

Methyl 5-*N*-Acetylamino-4-iodo-2-nitrobenzoate (1e). To a solution of **1d** (1.6 g, 4.97 mmol) in dichloromethane (15 mL) was added concentrated H_2SO_4 (0.85 mL) at 0 °C. After 5 min, a solution of acetic anhydride (1.17 mL, 12.38 mmol) in dichloromethane (5 mL) was added dropwise at 0 °C. Upon addition, the mixture was warmed to room temperature and stirred for 1 h until completion was detected by TLC. The resulting solution was washed with water, aqueous $NaHCO_3$, and brine, dried over anhydrous Na_2SO_4, and filtered. The resulting filtrate was evaporated in vacuo to yield a pale yellow solid, which was recrystallized from MeOH to afford 1.6 g (93.8%) of **1e** as a white solid. TLC, $R_f = 0.48$ (petroleum ether/EtOAc, 1/2). ^{1}H NMR (500 MHz, CDCl$_3$): δ 2.31 (s, 3H, Ac), 3.93 (s, 3H, MeO), 7.71 (b, 1H, NH), 8.44 (s, 1H, Ar−H), 8.67 (s, 1H, Ar−H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 25.56, 53.97, 89.43, 119.96, 130.55, 135.17, 142.45, 143.53, 166.02, 168.91.

Methyl 5-*N*-Acetylamino-4-iodo-2-aminobenzoate (1f). To a mixture of **1e** (5.6 g, 15.4 mmol) in absolute ethanol (88 mL) and glacial acetic acid (88 mL) was added iron powder (2.58 g, 46.7 mmol). The mixture was then heated to reflux for 2 h. The red reaction solution was allowed to cool to room temperature, diluted with water (300 mL), and extracted with dichloromethane (100 mL × 3). The combined organic extracts were then washed with water and dried over anhydrous Na_2SO_4. The solvent was removed in vacuo to provide a pale yellow solid, which was recrystallized from MeOH to afford 4.36 g (84.8%) of **1f** as a white needle. TLC, $R_f = 0.36$ (petroleum ether/EtOAc, 1/2). ^{1}H NMR (500 MHz, CDCl$_3$): δ 2.22 (s, 3H, Ac), 3.87 (s, 3H, MeO), 5.69 (b, 2H, NH$_2$), 7.06 (b, 1H, NH), 7.18 (b, 1H, Ar−H), 8.29 (s, 1H, Ar−H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 24.19, 51.81, 101.0, 111.24, 126.11, 126.26, 127.31, 148.29, 167.87, 168.43.

Methyl 5-*N*-Acetylamino-4-iodo-2-[3,3-diethyl-1-triazenyl] Benzoate (1g). A solution of sodium nitrite (0.49 g, 7.1 mmol) in water (4.5 mL) was cooled to 0 °C and then added dropwise over a 10 min period to a 0 °C solution of **1f** (2.13 g, 6.38 mmol) and concentrated hydrochloric acid (1.8 mL) in water (12 mL) and acetonitrile (20 mL). The mixture was stirred for 0.5 h at 0 °C and then added dropwise to a solution of diethylamine (2.33 mL, 22 mmol) and potassium carbonate (2.9 g, 21 mmol) which was precooled to 0 °C. During the addition, more diethylamine (2.3 mL) was added to the reaction solution. After addition, the mixture was warmed to room temperature for 0.5 h. During that period, a yellow solid precipitated. Upon completion, the solution was extracted with dichloromethane (80 mL × 2). The combined organic extracts were then washed with brine and water, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to yield a yellow solid, which was recrystallized from MeOH to afford 2.39 g (86.2%) of **1g** as a colorless needle. TLC, $R_f = 0.23$ (petroleum ether/EtOAc, 3/2). ^{1}H NMR (500 MHz, CDCl$_3$): δ 1.31 (b, 6H, Me), 2.24 (s, 3H, Ac), 3.74 (b, 4H, CH$_2$), 3.85 (s, 3H, MeO), 7.35 (b, 1H, NH), 7.86 (s, 1H, Ar−H), 8.41 (s, 1H, Ar−H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 11.09, 14.52, 24.71, 41.80, 49.20, 52.08, 93.94, 121.97, 127.15, 128.79, 134.63, 146.74, 167.83, 167.98.

5-*N*-Acetylamino-4-iodo-2-[3,3-diethyl-1-triazenyl] Benzoic Acid (1h). A solution of **1g** (1.4 g, 3.35 mmol) in MeOH (9 mL) was heated to reflux, to which was added dropwise aqueous NaOH (3.7 mL, 1 N). The resulting solution was refluxed for 0.5 h and then cooled to room temperature. Upon cooling, water (20 mL) was introduced. The solution was then extracted with Et$_2$O, and the water phase was neutralized to pH 3 with 1 N HCl. After filtration, the solid was dried in vacuo to afford 1.27 g (93.8%) of **1h** as a white solid. ^{1}H NMR (500 MHz, CDCl$_3$): δ 1.31 (t, 3H), 1.44 (t, 3H), 2.24 (s, 3H, Ac), 3.78 (q, 2H), 3.95 (q, 2H), 7.43 (s, 1H, NH), 8.12 (s, 1H, Ar−H), 8.71 (s, 1H, Ar−H), 13.96 (s, 1H, COOH). ^{13}C NMR (125 MHz, CDCl$_3$): δ 10.27, 14.36, 24.44, 43.47, 51.03, 98.62, 122.24, 125.98, 126.26, 135.98, 145.30, 166.34.

Octyl 5-*N*-Acetylamino-4-iodo-2-[3,3-diethyl-1-triazenyl] Benzoate (1i). A solution of the white acid **1h** (3.0 g, 7.43 mmol), DCC (1.6 g, 7.77 mmol), and DMAP (0.27 g, 2.21 mmol) in dichloromethane (40 mL) was stirred for 1 h at room temperature, to which were added *n*-octanol (1.11 g, 8.54 mmol) and more DCC (1.6 g, 7.77 mmol), respectively. The reaction mixture was stirred for 48 h at room temperature, filtered, and concentrated to give a red oil, which was purified by silica gel flash column chromatography (petroleum ether/EtOAc, 4/1) to provide 3.27 g (85.3%) of **1i** as a pale yellow oil. TLC, $R_f = 0.33$ (petroleum ether/EtOAc, 2/1). ^{1}H NMR (500 MHz, CDCl$_3$): δ 0.88 (t, 3H), 1.22−1.39 (m, 16H), 1.72 (m, 2H), 2.20 (s, 3H, Ac), 3.75 (b, 4H, CH$_2$), 4.23 (t, 2H, CH$_2$O), 7.42 (s, 1H, Ar−H), 7.87 (s, 1H, NH), 8.37 (s, 1H, Ar−H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 11.46, 14.33, 14.78, 22.88, 24.93, 26.12, 28.89, 29.39, 29.50, 32.03, 41.91, 49.40, 65.59, 94.02, 122.07, 127.97, 128.93, 134.83, 146.79, 167.85, 168.23.

Octyl 5-*N*-Acetylamino-2-[3,3-diethyl-1-triazenyl]-4-[2-(1,1-trimethylsilyl)-1-ethynyl] Benzoate (1k). A 50 mL flask under argon was charged with **1i** (0.77 g, 1.49 mmol), dichlorobis(triphenylphosphine) palladium(II) (21 mg, 0.030 mmol), copper(I) iodide (5.7 mg, 0.03 mmol), and triethylamine (23 mL). The solution was then stirred and warmed to 40 °C, to which was added dropwise degassed trimethylsilylacetylene (220 μL, 1.54 mmol) by syringe. The reaction mixture was allowed to stir for 12 h at the same temperature, filtered, and then concentrated to yield a dark oil. The oil was purified by flash silica gel column chromatography (petroleum/EtOAc, 8/1) to afford 0.68 g (93.8%) of **1k** as a colorless solid. TLC, $R_f = 0.39$ (petroleum ether/EtOAc, 5/1). ^{1}H NMR (500 MHz, CDCl$_3$): δ 0.30 (s, 9H, SiMe$_3$), 0.88 (t, 3H), 1.29 (b, 16H), 1.72 (m, 2H), 2.20 (s, 3H, Ac), 3.73 (b, 4H, CH$_2$), 4.26 (t, 2H, CH$_2$O), 7.49 (s, 1H, Ar−H), 7.92 (s, 1H, NH), 8.61 (s, 1H, Ar−H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 0.099, 11.89, 14.27, 14.33, 22.84, 24.94, 26.16, 28.89, 29.36, 29.47, 32.00, 41.97, 49.23, 65.54, 100.18, 103.35, 114.36, 119.21, 121.61, 128.69, 136.17, 145.05, 167.85, 168.09. Anal. Calcd for C$_{26}$H$_{42}$N$_4$O$_3$Si: C, 64.16; H, 8.70; N, 11.51. Found: C, 64.14; H, 8.60; N, 11.61.

Methyl 5-*N*-Acetylamino-2-[3,3-diethyl-1-triazenyl]-4-[2-(1,1-trimethylsilyl)-1-ethynyl] Benzoate (1j). Compound **1j** was prepared from **1g** (6.12 g, 14.64 mmol) as described for **1k** to afford a brown oil. The oil was purified by silica gel column chromatography (petroleum ether/EtOAc, 2/1) to afford 5.58 g (98.2%) of **1j** as a pale yellow solid. TLC, $R_f = 0.38$ (petroleum ether/EtOAc, 2/1). ^{1}H NMR (500 MHz, CDCl$_3$): δ 0.30 (s, 9H, SiMe$_3$), 1.26 (b, 6H, CH$_3$), 2.20 (s, 3H, Ac), 3.73 (b, 4H, CH$_2$), 3.86 (s, 3H, MeO), 7.49 (s, 1H, Ar−H), 7.92 (b, 1H, NH), 8.63 (s, 1H, Ar−H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 0.39, 11.09, 14.57, 25.26, 42.08, 49.83, 52.57, 100.4, 103.85, 114.92, 119.70, 121.96, 128.29, 136.41, 145.55, 168.19, 168.65. Anal. Calcd for C$_{19}$H$_{28}$N$_4$O$_3$Si: C, 58.73; H, 7.26; N, 14.42. Found: C, 58.77; H, 7.26; N, 14.48.

Methyl 5-*N*-Acetylamino-2-iodo-4-[2-(1,1-trimethylsilyl)-1-ethynyl] Benzoate (1l). To a sealed tube were added **1j** (2.39 g, 6.16 mmol) and iodomethane (10 mL) under argon. The mixture was stirred for 12 h at 120 °C. After filtration, the filtrate was concentrated to yield a brown oil, which was purified by silica gel column chromatography (petroleum ether/EtOAc, 3/1) to afford 2.09 g (81.9%) of **1m** as a white solid. TLC, $R_f = 0.53$ (petroleum ether/EtOAc, 2/1). ^{1}H NMR (500 MHz, CDCl$_3$): δ 0.31 (s, 9H, SiMe$_3$), 2.22 (s, 3H, Ac), 3.92 (s, 3H, MeO), 7.90 (s, 1H, Ar−H), 7.99 (s, 1H, Ar−H), 8.86 (s, 1H, Ar−H). ^{13}C NMR (125 MHz, CDCl$_3$): δ −0.041, 25.02, 52.90, 85.46, 97.90, 106.29, 116.10, 120.95, 136.03, 139.42, 143.37, 166.54, 168.25.

Octyl 5-*N*-Acetylamino-2-[3,3-diethyl-1-triazenyl]-4-ethynyl Benzoate (1m). To a solution of the compound **1k** (0.95 g, 1.95 mmol) in MeOH (15 mL) was added potassium carbonate (15 mg, 0.11 mmol) as described for **1l** to yield a brown oil. The oil was then purified by silica gel column chromatography (petroleum ether/EtOAc, 2/1) to afford 0.73 g (90.2%) of **1m** as a light yellow oil. TLC, $R_f = 0.48$ (petroleum ether/EtOAc, 1/1). ^{1}H NMR (500 MHz, CDCl$_3$): δ 0.87 (t, 3H), 1.26−1.38 (m, 16H), 1.72 (m, 2H), 2.20 (s, 3H, Ac), 3.55 (s, 1H), 3.72 (b, 4H), 7.54 (s, 1H, Ar−H), 7.91 (s, 1H, NH), 8.58 (s, 1H, Ar−H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 11.41, 14.28, 14.67,

22.83, 24.94, 25.98, 26.14, 28.85, 29.48, 31.98, 32.97, 41.80, 49.26, 63.06, 65.57, 79.08, 85.35, 113.56, 119.75, 122.40, 128.843, 136.17, 145.08, 168.18, 168.33.

Octyl 5-*N*-Acetylamino-2-iodo-4-[2-(1,1-trimethylsilyl)-1-ethynyl] Benzoate (1n). The compound was synthesized from **1k** (0.97 g, 1.99 mmol) by a procedure similar to that used for **1m** to yield a light yellow oil. The oil was then purified by silica gel column chromatography (petroleum ether/EtOAc, 15/1, 10/1) to afford a colorless oil, which was left standing overnight to afford 0.81 g (79.4%) of **1n** as a white wax. TLC, $R_f = 0.58$ (petroleum ether/EtOAc, 5/1). ^{1}H NMR (500 MHz, CDCl$_3$): δ 0.31 (s, 9H, SiMe$_3$), 0.88 (t, 3H), 1.29 (m, 10H), 1.78 (m, 2H), 2.22 (s, 3H, Ac), 4.32 (t, 2H, CH$_2$O), 7.91 (s, 1H, NH), 7.97 (s, 1H, Ar–H), 8.83 (s, 1H, Ar–H). ^{13}C NMR (125 MHz, CDCl$_3$): δ −0.032, 14.29, 22.83, 25.00, 26.11, 28.72, 28.85, 29.38, 31.97, 66.30, 85.25, 97.94, 106.08, 115.91, 120.83, 136.66, 139.43, 143.20, 166.32, 168.20.

2-[2-(2-Methoxyethoxy) ethoxy]ethyl 2-Iodobenzoate (1p). To a solution of 2-iodobenzoic acid (**1o**) (1.26 g, 5.08 mmol) and triethylamine (2.5 mL) in dichloromethane (20 mL) was added dropwise trimethylacetyl chloride (1.8 mL) at 0 °C. The reaction solution was allowed to warm to room temperature and stirred for 1 h. The solution was then cooled in an ice−water bath, to which a solution of triethyleneglycol monomethyl ether (1.05 g, 6.40 mmol) in dichloromethane (10 mL) was added dropwise. The reaction mixture was allowed to stir for 12 h at room temperature, washed with water, dried over Na$_2$SO$_4$, filtered, and concentrated to afford a red oil. The oil was purified by silica gel column chromatography (petroleum ether/EtOAc, 3/1) to afford 1.92 g (96.0%) of **1p** as a pale yellow oil. TLC, $R_f = 0.48$ (CHCl$_3$/acetone, 10/1). ^{1}H NMR (500 MHz, CDCl$_3$): δ 3.35 (s, 3H, MeO), 3.52 (m, 2H), 3.63−3.85 (m, 6H), 3.85 (t, 2H), 4.89 (t, 2H), 7.15 (m, 1H), 7.40 (m, 1H), 7.83 (d, 1H), 7.96 (d, 1H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 27.34, 59.16, 63.67, 64.80, 69.10, 70.78, 72.08, 94.29, 128.06, 131.26, 132.84, 15.19, 141.40, 166.51.

Methyl 5-*N*-Acetylamino-2-[3,3-diethyl-1-triazenyl]-4-ethynyl Benzoate (1q). To a solution of **1j** (0.50 g, 1.29 mmol) in methanol (8 mL) was added potassium carbonate (12 mg, 0.087 mmol). The solution was stirred for 5 min at room temperature, diluted with water (10 mL), and then extracted with dichloromethane (10 mL × 20). The pale yellow extracts were washed with water, dried over Na$_2$SO$_4$, and concentrated to yield an oil. The oil was purified by silica gel column chromatography (petroleum ether/EtOAc, 1/1) to afford 0.39 g (96.2%) of **1q** as a pale yellow solid. TLC, $R_f = 0.57$ (petroleum ether /EtOAc, 1/3). ^{1}H NMR (500 MHz, CDCl$_3$): δ 1.26 (m, 6H, CH$_3$), 2.22 (s, 3H, Ac), 3.53 (s, 1H, CCH), 3.72 (m, 4H, CH$_2$), 3.86 (s, H, MeO), 7.53 (s, 1H, Ar–H), 7.82 (s, 1H, NH), 8.62 (s, 1H, Ar–H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 25.02, 52.27, 79.18, 85.21, 113.54, 119.84, 122.50, 128.36, 136.20, 145.29, 168.11, 168.32.

Dimer 2e. The acetylene **1m** (0.74 g, 1.79 mmol), **1n** (0.76 g, 1.48 mmol), bis(dibenzylideneacetone) palladium (22 mg, 0.024 mmol), copper(I) iodide (4.7 mg, 0.024 mmol), and triphenylphosphine (33 mg, 0.12 mmol) in dry triethylamine (20 mL) were stirred at 70 °C for 24 h under argon. The reaction solution was then concentrated to yield a dark oil, which was purified by silica gel column chromatography (petroleum ether/EtOAc, 5/1) to afford 1.05 g (88.9%) of dimer **2e** as a yellow solid. TLC, $R_f = 0.63$ (petroleum ether/EtOAc, 2/1). ^{1}H NMR (500 MHz, CDCl$_3$): δ 0.33 (s, 9H, SiMe$_3$), 0.88 (m, 6H), 1.27−1.44 (m, 26H), 1.74 (m, 2H), 1.80 (m, 2H), 2.26 (s, 3H, Ac), 2.41 (s, 3H, Ac), 3.76 (m, 4H, CH$_2$), 4.27 (t, 2H), 4.33 (t, 2H), 7.55 (s, 1H), 7.75 (s, 1H), 8.03 (s, 1H), 8.84 (s, 1H), 9.16 (s, 1H), 9.22 (s, 1H). ^{13}C NMR (125 MHz, CDCl$_3$): δ −0.009, 14.33, 22.87, 24.74, 25.08, 26.13, 26.19, 28.74, 28.91, 29.38, 29.40, 29.43, 29.52, 31.99, 32.04, 65.53, 66.23, 90.41, 94.73, 98.43, 106.47, 114.17, 118.66, 119.62, 120.79, 121.69, 128.77, 131.33, 136.83, 137.80, 139.06, 144.63, 165.52, 168.32, 169.88.

Dimer 2f. To a solution of dimer **2e** (0.58 g, 0.72 mmol) in MeOH (8 mL) and dichloromethane (1 mL) was added potassium carbonate (5 mg, 0.026 mmol). The mixture was allowed to stir for 10 min at room temperature, and then water (8 mL) was added. Upon addition, the solution was extracted with dichloromethane (10 mL × 3), and the resulting organic extracts were then washed with water (10 mL), dried over Na$_2$SO$_4$, filtered, and concentrated to afford 0.51 g (96.5%) of dimer **2f** as a pure pale yellow oil. TLC, $R_f = 0.39$ (petroleum ether/EtOAc, 1/3). ^{1}H NMR (500 MHz, CDCl$_3$): δ 0.88 (m, 6H), 1.28−1.45 (m, 26H), 1.78 (m, 4H), 2.26 (s, 3H, Ac), 2.40 (s, 3H, Ac), 3.66 (s, 1H, CCH), 3.74 (b, 4H), 4.27 (m, 4H, CH$_2$O), 7.52 (s, 1H, Ar–H), 7.74 (s, 1H, Ar–H), 7.96 (s, 1H, NH), 8.84 (s, 1H, Ar–H), 9.12 (s, 1H, NH), 9.18 (s, 1H, Ar–H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 14.27, 22.84, 24.69, 25.04, 26.11, 28.73. 28.91, 29.35, 29.37, 29.41, 29.49, 31.97, 32.01, 65.51, 66.22, 77.72, 87.54, 90.42, 94.60, 114.10, 114.90, 118.68, 119.60, 121.36, 121.74, 128.81, 131.61, 137.44, 137.79, 139.32, 144.59, 165.42, 168.37, 168.60, 169.82.

Dimer 2. A mixture of the acetylene **1q** (78 mg, 0.25 mmol), **1p** (112 mg, 0.28 mmol), bis(dibenzylideneacetone) palladium (4.6 mg, 0.0053 mmol), copper(I) iodide (1 mg, 0.0052 mmol), and triphenylphosphine (6.9 mg, 0.025 mmol) in triethylamine (15 mL) was heated at 70 °C under argon for 12 h. The solution was concentrated to yield a brown oil, which was purified by PTLC (CH$_2$Cl$_2$/acetone, 10/1) to afford 130 mg (89.1%) of **2** as a yellow solid. TLC, $R_f = 0.34$ (CHCl$_3$/acetone, 8/1). ^{1}H NMR (500 MHz, CDCl$_3$): δ 1.28 (m, 6H), 2.40 (s, 3H, Ac), 3.36 (s, MeO, 3H), 3.52 (t, CH$_2$O, 2H), 3.63−3.76 (m, 10H), 3.87 (m, 5H), 4.48 (t, CH$_2$O, 2H), 7.43 (t, 1H), 7.58 (m, 2H), 7.71 (d, 1H, $J = 7.5$ Hz), 8.15 (d, 1H, $J = 8.0$ Hz), 8.87 (s, 1H), 9.27 (s, 1H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 24.76, 52.22, 59.22, 64.85, 69.18, 70.82, 70.86, 70.99, 72.13, 90.79, 95.60, 114.50, 119.89, 122.02, 124.17, 128.14, 128.55, 130.21, 131.13, 132.73, 134.21, 137.77, 144.90, 165.85, 168.54, 169.77.

Trimer 3. Following the coupling procedure as described for **2e**, the mixture of the acetylene **2f** (139 mg, 0.19 mmol), **1p** (102 mg, 0.26 mmol), bis(dibenzylideneacetone) palladium (3.5 mg, 0.0038 mmol), copper(I) iodide (1 mg, 0.0052 mmol), and triphenylphosphine (5.2 mg, 0.019 mmol) in triethylamine (10 mL) was heated at 70 °C under argon for 5 h. The solution was then filtered and concentrated to yield a dark oil, which was purified by silica gel column chromatography (dichloromethane/MeOH, 30/1, 20/1) to afford 131 mg (69.4%) of **3** as a yellow solid. TLC, $R_f = 0.45$ (CHCl$_3$/acetone, 10/1). ^{1}H NMR (500 MHz, CDCl$_3$): δ 0.88 (s, 6H), 1.39 (m, 26H), 1.74 (m, 2H), 1.82 (m, 2H), 2.42 (s, 3H, Ac), 2.45 (s, 3H, Ac), 3.36 (s, 3H, MeO), 3.53 (m, 2H), 3.67−3.76 (m, 10H), 3.87 (t, 2H), 4.27(t, 2H), 4.32 (t, 2H), 4.49 (t, 2H), 7.49 (t, 1H), 7.58 (s, 1H), 7.85 (s, 1H, Ar–H), 7.62 (t, 1H), 7.72 (d, 1H, $J = 7.5$ Hz), 8.17 (d, 1H, $J = 8.0$ Hz), 8.86 (s, 1H), 9.27 (s, 1H), 9.38 (s, 1H), 9.45 (s, 1H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 14.09, 22.65, 24.49, 24.54, 24.63, 24.68, 25.92, 25.97, 28.56, 28.70, 29.17, 29.22, 29.30, 31.79, 31.82, 59.06, 64.79, 65.28, 65.94, 68.94, 70.65, 70.68, 70.82, 71.94, 89.01, 89.85, 94.79, 97.40, 114.15, 115.57, 117.90, 121.25, 121.46, 121.52, 123.39, 128.44, 130.20, 131.09, 131.20, 132.73, 134.12, 136.84, 136.88, 137.62, 140.57, 144.45, 165.56, 165.69, 168.08, 169.68, 170.11. Anal. Calcd for C$_{56}$H$_{75}$N$_5$O$_{11}$: C, 67.65; H, 7.60; N, 7.04. Found: C, 67.80; H, 7.63; N, 7.09.

Trimer 3a. To a sealed tube were added trimer **3** (0.23 g, 0.23 mmol) and iodomethane (1.5 mL). The mixture was stirred for 24 h at 120 °C to yield a brown residue. The residue was then purified by silica gel column chromatography (dichloromethane/MeOH, 15/1, 10/1) to afford 173 mg (73.7%) of **3a** as a yellow solid. TLC, $R_f = 0.52$ (CHCl$_3$/acetone, 10/1). ^{1}H NMR (500 MHz, CDCl$_3$): 0.88 (m, 6H), 1.29−1.46 (m, 20H), 1.81 (m, 4H), 2.41 (s, 3H, Ac), 2.44 (s, 3H, Ac), 3.36 (s, 3H, MeO), 3.52 (t, 2H), 3.64−3.73 (m, 6H), 3.88 (t, 2H), 4.31 (m, 4H), 4.46 (m, 2H), 7.47 (t, 1H, Ar–H), 7.59 (t, 1H, Ar–H), 7.67 (d, 1H, $J = 7.5$ Hz), 7.75 (s, 1H, Ar–H), 8.01 (s, 1H, Ar–H), 8.15 (d, 1H, $J = 8$ Hz), 9.08 (s, 1H, Ar–H), 9.27 (s, 1H, NH), 9.38 (s, 1H, Ar–H), 9.40 (s, 1H, NH). ^{13}C NMR (125 MHz, CDCl$_3$): δ 14.33, 22.87, 24.78, 24.81, 24.89, 26.13, 26.12, 28.72, 29.39, 29.43, 32.00, 32.02, 59.24, 59.27, 65.01, 66.18, 66.22, 69.11, 70.85, 71.00, 72.12, 84.79, 87.83, 88.95, 97.20, 97.94, 115.87, 116.17, 117.31, 121.40,

123.43, 129.17, 130.13, 131.11, 131.31, 132.98, 134.39, 135.87, 137.20, 140.96, 141.19, 143.27, 165.57, 165.73, 166.39, 170.30, 170.36.

Tetramer 4. Following the coupling procedure as described for trimer **3**, compound **1m** (31 mg, 0.075 mmol), trimer **3a** (51 mg, 0.050 mmol), bis(dibenzylideneacetone) palladium (1 mg, 0.0011 mmol), copper(I) iodide (0.5 mg, 0.0026 mmol), and triphenylphosphine (1.5 mg, 0.0056 mmol) in triethylamine (15 mL) were heated at 70 °C under argon for 28 h. The solution was filtered and concentrated to give a dark oil, which was purified by silica gel column chromatography (dichloromethane/acetone, 10/1) to give 48.5 mg (74.3%) of **4** as a yellow solid. TLC, R_f = 0.53 (CHCl$_3$/acetone, 5/1). ^{1}H NMR (500 MHz, CDCl$_3$): δ 0.88 (m, 9H), 1.29–1.46 (m, 36H), 1.76 (m, 2H), 1.83 (m, 4H), 2.42 (s, 3H, Ac), 2.47 (s, 6H, Ac), 3.37 (s, 3H, MeO), 3.53 (m, 2H), 3.65–3.89 (m, 12H), 4.27 (m, 2H, CH$_2$O), 4.33 (m, 4H, CH$_2$O), 4.51 (t, 2H), 7.51 (t, 1H, Ar—H, J = 8 Hz), 7.57 (s, 1H), 7.63 (t, 1H), 7.75 (d, 1H, J = 7 Hz), 7.82 (s, 1H), 7.86 (s, 1H), 8.20 (d, 1H, J = 7 Hz), 8.86 (s, 1H), 9.29 (s, 1H), 9.39 (s, 1H), 9.42 (s, 1H), 9.46 (s, 1H), 9.49 (s, 1H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 14.12, 22.66, 24.54, 24.62, 24.71, 25.92, 25.98, 28.54, 28.55, 28.70, 29.18, 29.24, 29.31, 31.80, 31.83, 59.07, 64.84, 65.29, 65.92, 66.09, 68.93, 70.65, 70.67, 70.82, 71.92, 88.17, 88.78, 89.69, 94.92, 97.14, 97.71, 114.22, 115.74, 115.77, 117.12, 117.82, 119.47, 121.22, 121.35, 121.53, 123.25, 128.33, 129.01, 130.14, 130.90, 131.14, 131.25, 132.74, 134.15, 136.60, 136.89, 137.00, 137.65, 140.54, 141.11, 144.41, 165.56, 165.66, 168.11, 169.76, 170.25, 170.27. Anal. Calcd for C$_{75}$H$_{98}$N$_6$O$_{14}$: C, 68.89; H, 7.55; N, 6.43. Found: C, 68.66; H, 7.56; N, 6.40.

Pentamer 5. A mixture of dimer **2f** (47 mg, 0.065 mmol), trimer **3a** (50.9 mg, 0.05 mmol), bis(dibenzylideneacetone) palladium (2 mg, 0.0022 mmol), copper(I) iodide (0.5 mg, 0.0026 mmol), and triphenylphosphine (3.1 mg, 0.012 mmol) in triethylamine (10 mL) was stirred at 70 °C under argon for 28 h. After removal of solvent, the resulting residue was purified by silica gel PTLC (dichloromethane/acetone, 10/1) to afford 64 mg (60.8%) of yellow solid **5**. TLC, R_f = 0.47 (CHCl$_3$/acetone, 5/1). ^{1}H NMR (500 MHz, CDCl$_3$): δ 0.88 (s, 12H), 1.32 (m, 46H), 1.73 (m, 2H), 1.83 (m, 6H), 2.42 (s, 3H, Ac), 2.48 (s, 9H), 3.37 (s, 3H), 3.55 (t, 2H), 3.73 (m, 10 H), 3.89 (m, 2H), 4.32 (m, 8H), 4.49 (t, 2H), 7.41 (t, 1H), 7.46 (t, 1H), 7.51 (s, 1H), 7.63 (d, 1H, J = 8.0 Hz), 7.75 (s, 1H), 7.78, 7.80 (d, 2H), 8.15 (d, 1H, J = 7.5 Hz), 8.82 (s, 1H), 9.20 (s, 1H), 9.33, 9.36, 9.38, 9.39 (q, 4H), 9.42 (s, 1H), 9.43 (s, 1H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 14.12, 22.68, 24.68, 24.75, 25.96, 28.58, 28.74, 29.21, 29.29, 29.33, 31.83, 59.05, 64.88, 65.25, 65.92, 66.08, 66.14, 68.96, 70.67, 70.70, 70.84, 71.96, 87.95, 88.03, 88.71, 89.59, 94.82, 95.01, 97.29, 97.48, 97.75, 114.25, 115.74, 115.80, 115.92, 117.02, 117.08, 117.78, 119.40, 121.08, 121.19, 121.28, 121.37, 121.44, 123.19, 128.32, 130.01, 130.69, 130.81, 131.08, 131.15, 132.60, 136.60, 136.89, 137.10, 140.59, 141.07, 141.22, 144.28, 165.45, 165.58, 168.03, 169.75, 170.25, 170.27, 170.35. Anal. Calcd for C$_{94}$H$_{121}$N$_7$O$_{17}$: C, 69.65; H, 7.52; N, 6.05. Found: C, 69.43; H, 7.55; N, 5.90.

Dimer 2g. A mixture of **1l** (0.52 mg, 1.25 mmol), **1m** (0.58 g, 1.40 mmol), bis(dibenzylideneacetone) palladium (21 mg, 0.023 mmol), copper(I) iodide (4.4 mg, 0.023 mmol), and triphenylphosphine (31 mg, 0.12 mmol) in triethylamine (30 mL) was stirred at 70 °C under argon for 12 h. The solution was then filtered and concentrated to yield a brown residue, which was purified by silica gel column (petroleum/EtOAc, 3/2) to afford 0.81 g (92.4%) of the dimer **2g** as a yellow solid. TLC, R_f = 0.43 (petroleum ether/EtOAc, 1/1). ^{1}H NMR (500 MHz, CDCl$_3$): δ 0.33 (s, 9H, SiMe$_3$), 0.88 (t, 3H), 1.29 (m, 16 H), 1.74 (t, 2H, CH$_2$), 2.25 (s, 3H, Ac), 2.42 (s, 3H, Ac), 3.75 (b, 4H, CH$_2$), 3.94 (s, 3H, MeO), 4.27 (t, 2H, CH$_2$O), 7.54 (s, 1H, Ar—H), 7.75 (s, 1H, Ar—H), 8.03 (s, 1H, NH), 8.88 (s, 1H, Ar—H), 9.12 (s, 1H, Ar—H), 9.21 (s, 1H, NH). ^{13}C NMR (125 MHz, CDCl$_3$): δ −0.032, 14.29, 22.85, 24.72, 25.03, 26.18, 28.91, 29.38, 29.50, 32.02, 52.89, 65.50, 90.50, 94.61, 98.40, 106.57, 114.10, 118.76, 119.64, 120.90, 120.90, 121.71, 128.86, 130.84, 136.84, 137.79, 139.03, 144.62, 165.94,

168.29, 168.35, 169.81. Anal. Calcd for C$_{38}$H$_{51}$N$_5$O$_6$Si: C, 65.02; H, 7.32; N, 9.98. Found: C, 64.87; H, 7.22; N, 10.13.

Dimer 2h. To a solution of the dimer **2g** (0.57 g, 0.81 mmol) in MeOH (10 mL) was added potassium carbonate (6 mg, 0.043 mmol), and the reaction was carried out as described for **2f** to afford 0.46 g (90.2%) of the desired **2h** as a yellow oil. TLC, R_f = 0.55 (petroleum ether/EtOAc, 1/3). ^{1}H NMR (500 MHz, CDCl$_3$): δ 0.88 (t, 3H), 1.29 (m, 16 H), 1.74 (m, 2H), 2.26 (s, 3H, Ac), 2.42 (s, 3H, Ac), 3.65 (s, 1H, CCH), 3.74 (b, 4H, CH$_2$), 3.93 (s, 3H, MeO), 4.27 (b, 2H, CH$_2$O), 7.52 (s, 1H, Ar—H), 7.73 (s, 1H, Ar—H), 7.95 (s, 1H, NH), 8.83 (s, 1H, Ar—H), 9.09 (s, 1H, Ar—H), 9.16 (s, 1H, NH). ^{13}C NMR (125 MHz, CDCl$_3$): δ 14.27, 22.84, 24.71, 25.04, 26.18, 28.91, 29.37, 29.49, 32.01, 52.90, 65.54, 77.67, 87.61, 90.48, 94.54, 114.05, 115.11, 119.78, 119.58, 121.45, 121.75, 128.85, 131.06, 137.47, 139.26, 144.56, 165.83, 168.42, 168.64, 169.85.

Trimer 3b. A mixture of **2h** (263 mg, 0.42 mmol), **1n** (300 mg, 0.58 mmol), bis(dibenzylideneacetone) palladium (7.6 mg, 0.0083 mmol), copper(I) iodide (2 mg, 0.01 mmol), and triphenylphosphine (15 mg, 0.056 mmol) in dry triethylamine (28 mL) was stirred at 70 °C under argon for 24 h. The solution was then filtered and concentrated to yield a brown oil, which was purified by silica gel column (petroleum ether/dichloromethane/MeOH, 3/1/0.5) to afford 280 mg (66.0%) of **3b** as a yellow oil. TLC, R_f = 0.51 (petroleum ether/CHCl$_3$/acetone, 1/1/0.5). ^{1}H NMR (500 MHz, CDCl$_3$): 0.88 (m, 6H), 1.29–1.46 (m, 26H), 1.75 (t, 2H), 1.81 (t, 2H), 2.26 (s, 3H, Ac), 2.42 (s, 6H, Ac), 3.75 (b, 4H), 3.92 (s, 3H, MeO), 4.29 (m, 4H, CH$_2$O), 7.54 (s, 1H, Ar—H), 7.73 (b, 2H, Ar—H), 8.01 (s, 1H, NH), 8.87 (s, 1H, Ar—H), 9.17 (s, 1H), 9.22 (s, 1H, NH), 9.32 (s, 1H, NH), 9.34 (s, 1H, Ar—H). ^{13}C NMR (125 MHz, CDCl$_3$): δ −0.05, 14.28, 22.85, 24.74, 24.79, 25.00, 26.12, 26.18, 28.71, 28.92, 29.35, 29.38, 29.42, 29.50, 31.97, 32.02, 52.82, 65.47, 66.35, 88.58, 89.97, 94.96, 97.15, 98.18, 106.76, 114.27, 115.95, 116.03, 117.84, 118.11, 119.59, 120.96, 121.39, 121.74, 128.66, 130.57, 136.91, 137.82, 139.64, 140.66, 144.58, 165.41, 166.11, 168.30, 168.39, 169.89, 170.38.

Hexamer 6. To a solution of **3b** (30 mg, 0.029 mmol) in MeOH (3 mL) was added potassium carbonate (0.5 mg, 0.0036 mmol). The reaction solution was stirred for 10 min at room temperature, and then water (5 mL) was introduced. Upon addition, the mixture was extracted with chloroform (5 mL × 3), and the combined organic extracts were washed with water, dried over Na$_2$SO$_4$, and concentrated to yield 26 mg of a yellow oil. The oil was a single spot on a TLC plate and was used for the next step without purification. To the above oil (26 mg, 0.028 mmol) were added trimer **3a** (21.5 mg, 0.021 mmol), bis-(dibenzylideneacetone) palladium (0.8 mg, 0.87 μmol), copper(I) iodide (0.5 mg, 2.6 μmol), triphenylphosphine (2.1 mg, 0.008 mmol), and triethylamine (20 mL). The reaction mixture was then stirred at 70 °C under argon for 24 h. After removal of solvent, the resulting residue was purified by PTLC (chloromethane/acetone, 10/1) to afford 28 mg (72.7%) of hexamer **6** as a yellow solid. TLC, R_f = 0.45 (CHCl$_3$/acetone, 3/1). ^{1}H NMR (500 MHz, CDCl$_3$): δ 0.88–0.96 (m, 18H), 1.13 (b, 3H), 1.26–1.40 (m, 40H), 1.49 (m, 3H), 1.65 (m, 2H), 1.86 (m, 6H), 2.44–47 (m, 15H, Ac), 3.22 (b, 2H), 3.37 (s, 3H, MeO), 3.53 (m, 4H), 3.65 (m, 2H), 3.69 (m, 2H), 3.73 (m, 2H), 3.88 (t, 2H), 3.93 (s, 3H, MeO), 3.94 (s, 3H), 4.14 (t, 2H, J = 5 Hz), 4.31 (m, 6H), 4.45 (t, 2H, J = 4 Hz), 6.87 (b, 1H, Ar—H), 7.08 (b, 1H, Ar—H), 7.38 (b, 2H), 7.69 (s, 1H, Ar—H), 7.73 (s, 1H, Ar—H), 7.80 (s, 1H, Ar—H), 7.82 (s, 1H, Ar—H), 7.98 (d, 1H, Ar—H, J = 7.5 Hz), 8.75 (s, 1H, Ar—H), 8.95 (b, 1H), 9.05 (m, 3H), 9.23 (b, 1H), 9.37 (s, 1H), 9.42 (ts, 3H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 14.11, 14.14, 22.66, 22.71, 24.65, 24.72, 25.75, 26.01, 28.54, 28.56, 28.68, 29.22, 29.32, 29.38, 29.39, 31.83, 31.86, 52.64, 59.01, 64.86, 64.98, 66.08, 66.13, 66.22, 68.96, 70.64, 70.66, 70.76, 71.93, 78.03, 87.69, 87.74, 87.79, 88.09, 89.51, 94.43, 97.34, 97.68, 97.73, 97.98, 113.58, 115.77, 115.79, 115.85, 115.89, 117.02, 117.12, 117.85, 118.65, 120.62, 120.79, 122.69, 128.52, 129.09, 129.45, 130.05, 130.11, 130.24, 130.65, 132.20, 134.29, 136.80,

137.19, 137.47, 140.39, 140.97, 141.11, 143.48, 164.76, 164.81, 164.89, 164.99, 165.50, 167.94, 169.87, 170.27, 170.32, 170.40, 170.45. Anal. Calcd for $C_{106}H_{130}N_8O_{20}$: C, 69.33; H, 7.14; N, 6.10. Found: C, 69.26; H, 7.21; N, 5.87.

Heptamer 7. To a sealed tube fitted with a magnetic stirring bar were added **5a** (24 mg, 1.30×10^{-2} mmol), **2i** (31 mg, 3.90×10^{-2} mmol), Pd(dba)$_3$ (3.1 mg, 3.90×10^{-3} mmol), CuI (ca. 0.8 mg, 4.20×10^{-3} mmol), Ph$_3$P (1.5 mg, 5.72×10^{-3} mmol), and a mixed dry solvent of acetonitrile/triethylamine (2:1) (3 mL). The mixture was degassed three times, back-filled with nitrogen, and gradually heated. At ∼60 °C, the tube was sealed and allowed to react for 2 days at 75 °C. After being cooled to room temperature, the mixture was diluted with methanol, filtered, and concentrated. The brown residue was dissolved in a mixed solvent of CHCl$_3$/EtAc/MeOH (10:1:0.5) and subjected to flash chromatography with gradient elution (10:1:0.5, 10:1:0.8, 10:1:1, and 10:1:1.2). After several impurity bands, the last yellow band was collected (R_f: 0.15; developing agent, CHCl$_3$/EtAc/ MeOH 10:1:1.2), and a faint-brown solid was provided after removing the solvent (7.1 mg, 21.7%). The ^{1}H NMR spectrum in CDCl$_3$ showed a broad signal in the amide and aromatic region. ^{1}H NMR (500 MHz, DMSO-d_6/CD$_3$OD(60/40)): δ 7.25−6.68 (br, 15H, Ar), 4.40 (br, overlapped, CH$_2$), 3.50−3.70 (br, CH$_2$), 3.26 (m, 21H, CH$_3$), 2.60 (m, 18H, Ac), 2.27 (s, 3H, Ac), 1.28 (br, 6H, CH$_3$). MS *m/z* calcd for $C_{128}H_{158}N_{10}O_{42}$ (M$^+$) 2507.05; found (M + 2H)$^{2+}$ 1255; (M + H + Na)$^{2+}$ 1266; (M + 2Na)$^{2+}$ 1277.

Ab Initio and Molecular Mechanics Calculations. The ab initio computations were carried out using the Gaussian 98 revision A.9 program. The geometry of each conformation was optimized at the B3LYP/6-31G(d,p) level. The two optimized structures were used to compute the single-point energy at the MP2/6-31G(d) level. One of the C−Ph bonds of the optimized conformer **2a′** was rotated 180° to obtain the structure of conformer **2c′**. The same was done for conformer **2c′** to obtain a structure of **2a′**.

Molecular mechanics calculations were carried out using the CaChe program (version 3.22). Energy-minimized conformations of the corresponding tetramer, pentamer, and hexamer were obtained using the MM3 force field.

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